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Evaluation of Late-Onset Sarcopenia Following Radiotherapy in Mastectomy Patients

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A B S T R A C T

Introduction: Post-mastectomy radiation therapy is crucial for breast cancer management, yet its long-term impact on skeletal muscle depletion remains poorly understood. Because thoracic irradiation can provoke systemic catabolic pathways and progressive muscle loss, identifying secondary body composition changes is clinically vital. Therefore, this study was designed to evaluate the incidence of sarcopenia following radiotherapy in mastectomy patients.

Material and methods: This descriptive cross-sectional study evaluated 125 post-mastectomy patients recruited via convenience sampling at Shahid Madani Hospital. Following institutional ethics approval, standardized clinical data, radiotherapy records, and sarcopenia assessments including handgrip strength and muscle mass metrics were collected. Data were analyzed using appropriate descriptive and inferential statistical methods to examine post-treatment muscle status.

Results: In this cohort of 125 mastectomy patients, the overall prevalence of sarcopenia was 32.8% (n=41). Sarcopenic patients exhibited significantly lower appendicular skeletal muscle index (5.08±0.41 vs. 6.18±0.58 kg/m^2, P<0.001), reduced handgrip strength (14.4±2.5 vs. 20.8±3.7 kg, P<0.001), more extensive regional nodal irradiation (73.2% vs. 52.4%, P=0.019), and a longer post-radiotherapy interval (9.2±4.3 vs. 6.5±3.2 months, P<0.001), with time showing a significant inverse correlation with muscle mass (r=-0.38, P<0.001).

Conclusion: Post-mastectomy radiotherapy, particularly comprehensive regional nodal irradiation and extended post-treatment duration, is significantly associated with a high prevalence of sarcopenia and progressive skeletal muscle depletion. These findings underscore the critical clinical necessity for routine muscle mass screening and targeted rehabilitation protocols in survivors undergoing locoregional radiotherapy.

Introduction

Breast cancer remains the most diagnosed malignant neoplasm and one of the principal causes of cancer-related mortality among women worldwide, posing a sustained public health challenge across diverse demographic populations. Over the past three decades, coordinated improvements in population-wide mammographic screening, systematic biomarker profiling, and individualized treatment planning have substantially reduced disease-specific mortality and extended long-term overall survival metrics. Contemporary management integrates comprehensive multimodal regimens including primary surgical ablation, cytotoxic chemotherapy, endocrine therapy, targeted biologics, and adjuvant ionizing radiation to eradicate residual locoregional

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focus and prevent distant micro metastatic dissemination. However, the resulting expansion of the breast cancer survivorship community has fundamentally shifted the broader therapeutic paradigm beyond simple recurrence-free survival toward preserving functional autonomy, nutritional reserves, and long-term health-related quality of life [1].

Within local management strategies, total or modified radical mastectomy remains an indispensable surgical modality for women presenting with multicentric tumors, inflammatory breast carcinoma, elevated tumor-to-breast volumetric ratios, or explicit contraindications to breast-conserving surgery. Although modern mastectomy techniques are refined to minimize intraoperative morbidity, the procedure inevitably entails extensive physical, anatomical, and biomechanical trauma to the anterior chest wall and axilla. Surgical excision of glandular, fascial, and regional muscular tissues severs regional neurovascular structures and interrupts critical lymphatic channels, inducing a robust neuroendocrine and immunological stress response. The resultant surgical site pain, restricted upper extremity mobility, and postoperative physical inactivity together alter local metabolic homeostasis and initiate an early systemic catabolic state that impairs muscle tissue maintenance [2].

Following definitive surgical extirpation, post-mastectomy radiation therapy (PMRT) represents a cornerstone adjuvant intervention indicated for individuals exhibiting elevated risk factors for locoregional recurrence, such as advanced primary tumor stage, deep fascial margin involvement, and extensive axillary nodal metastasis. Landmark prospective randomized trials and long-term meta-analyses have established that PMRT lowers locoregional failure rates by up to two-thirds and produces measurable gains in overall survival. Contemporary radiation oncology employs computerized three-dimensional conformal radiation therapy and intensity-modulated radiation therapy to sculpt dose delivery to the reconstructed or native chest wall and regional lymphatic basins. Despite these advancements in beam conformality and normal tissue avoidance, surrounding skeletal musculature, including the pectoralis major and minor, serratus anterior, intercostal muscles, and adjacent periscapular compartments, unavoidably absorbs notable doses of ionizing radiation [3].

Sarcopenia, traditionally recognized as an involuntary, age-related decline in skeletal muscle mass, strength, and physical performance, is increasingly acknowledged as an acquired secondary phenomenon in oncological settings. Unlike classic physiological senile muscle loss, secondary cancer-associated sarcopenia frequently develops through accelerated multifactorial mechanisms driven by tumor burden, persistent systemic inflammation, nutritional depletion, and therapeutic interventions.

Within oncology populations, pre-existing or acquired low skeletal muscle index correlates strongly with an increased rate of severe chemotherapeutic adverse events, protracted wound-healing complications, impaired cardiorespiratory functional reserve, and truncated overall survival. Standardized single-slice computed tomography analysis, typically quantified at the third lumbar vertebra or chest-level cross sections, has emerged as the definitive modality for non-invasive, objective skeletal muscle quantification and body composition monitoring in longitudinal oncology cohorts [4].

The fundamental biological mechanisms responsible for muscle tissue degradation and contractile impairment following ionizing radiation exposure involve complex cellular and metabolic disruptions. Ionizing radiation acts on exposed tissue beds through targeted deoxyribonucleic acid strand breaks and the prolonged intracellular overproduction of reactive oxygen species. This localized oxidative stress overwhelms endogenous antioxidant scavenging systems, triggering membrane lipid peroxidation, structural myofibrillar protein damage, and profound mitochondrial bioenergetic failure within myocytes. Furthermore, sustained oxidative stress depletes the resident population of myogenic satellite cells by inducing permanent cellular senescence or apoptosis, thereby abrogating the intrinsic self-renewal and regenerative repair machinery required to replace damaged muscle fibers and preserve physiological muscular architecture [5].

Simultaneously, therapeutic radiation triggers a chronic profibrotic signaling cascade that severely alters the structural composition and microvascular environment of the exposed musculature. Radiation-induced endothelial apoptosis and subendothelial proliferation led to microvascular rarefaction, capillary obliteration, and luminal thrombosis, creating an environment of perpetual hypoxia and reduced nutrient delivery. Quiescent resident fibroblasts and infiltrating immune cells differentiate into persistently active myofibroblasts under continuous paracrine and autocrine stimulation driven by transforming growth factor-beta and inflammatory cytokines. Over extended follow-up intervals, soft, functional myofibrillar elements are progressively replaced by dense, non-compliant collagenous extracellular matrix, leading directly to macroscopic muscle shrinkage, tissue contracture, reduced range of motion, and persistent regional functional compromise [6].

In addition to direct localized parenchymal damage, ionizing radiation induces systemic physiological consequences through the continuous release of circulating inflammatory mediators into the systemic circulation. Irradiated thoracic tissues

continuously generate and shed pro-inflammatory cytokines, prominently including tumor necrosis factor-alpha, interleukin-1, and interleukin-6, into the peripheral bloodstream. These systemic factors stimulate signaling pathways such as nuclear factor-kappa B and p38 mitogen-activated protein kinase within distal, non-irradiated skeletal muscle groups. Persistent activation of these catabolic transcriptional programs drives the overactivation of the muscle-specific ubiquitin-proteasome pathway and excessive autophagic-lysosomal degradation, resulting in accelerated breakdown of structural myofibrillar proteins and contributing to widespread, systemic skeletal muscle wasting [7].

The diagnostic recognition of progressive muscle loss in breast cancer patients is frequently masked by the prevalent phenomenon of sarcopenic obesity. In contrast to cachexia patterns characterized by obvious systemic wasting, patients with breast cancer undergoing curative-intent adjuvant therapy frequently maintain or gain weight throughout the therapeutic continuum. This stable or increased body mass index can mask severe, concurrent reductions in metabolically active skeletal muscle mass behind enlarged subcutaneous and visceral adipose depots. Patients presenting with this concealed phenotype experience substantial intramuscular and intermuscular lipid infiltration termed my steatosis which degrades muscular quality and mechanical efficiency while increasing systemic insulin resistance and systemic inflammation. Routine anthropometric measures such as total body weight and body mass index fail to detect this covert wasting, leading to the clinical underestimation of physical frailty [8].

The metabolic and muscular challenges faced by mastectomy patients are further amplified by systemic therapeutic modalities administered prior to, concurrently with, or immediately after PMRT. Standard adjuvant chemotherapy regimens incorporating anthracyclines, taxanes, and alkylating agents induce profound, generalized mitochondrial toxicity, disrupt muscle protein synthesis, and provoke severe physical lethargy and functional disuse. Concurrently, long-term adjuvant endocrine therapies, including selective estrogen receptor modulators and third-generation aromatase inhibitors, induce prolonged estrogen deprivation that suppresses normal anabolic signaling pathways and elevates systemic bone and skeletal muscle turnover. When combined with persistent cancer-related fatigue, localized postoperative pain syndromes, and emotional distress, these overlapping treatment exposures form a continuous cycle of physical inactivity, progressive neuromuscular deconditioning, and systemic lean mass depletion [9].

Despite the established clinical prognostic value of baseline sarcopenia across diverse gastrointestinal and genitourinary cancers, the specific longitudinal trajectory and post-radiotherapy incidence of skeletal muscle wasting in mastectomy patients remain inadequately defined. Most available breast oncology investigations have evaluated muscle metrics cross-sectionally at initial diagnosis or immediately prior to chemotherapy, leaving the isolated, longitudinal impact of adjuvant radiation therapy on skeletal muscle homeostasis unexamined. Systematic prospective studies that combine serial standardized radiological assessments, rigorous volumetric dosimetric parameters, and validated clinical performance metrics are required to characterize post-radiation musculoskeletal changes and establish their functional implications. Addressing this knowledge gap is essential to identify high-risk individuals early and to formulate targeted prehabilitation, nutritional, and pharmacologic interventions that preserve physiological independence and long-term survivorship outcomes. Therefore, the primary objective of this study was to conduct an evaluation of sarcopenia incidence following radiotherapy in mastectomy patients.

Material and methods

Study Design:

This descriptive cross-sectional study was conducted at Shahid Madani Hospital in Tabriz, Iran, among women who had undergone mastectomy followed by radiotherapy for breast cancer. Each participant was assessed once after completing radiotherapy. The primary outcome was the proportion of participants meeting the prespecified diagnostic criteria for sarcopenia at that assessment. Because measurements were obtained at a single post-treatment time point, the study was designed to describe post-radiotherapy sarcopenia and its associations with clinical characteristics, rather than to establish that radiotherapy caused new-onset sarcopenia.

Sampling and Sample Size:

The sample size was estimated using Cochran's single-proportion formula, $n=Z1-\alpha/22p(1-p)/d2$. In the absence of a reliable prior estimate for this study population, the expected proportion was set at 0.50. With a 95% confidence level ($Z=1.96$) and an absolute precision of 0.088, the calculated sample size was 124.02, which was rounded up to 125 participants. Eligible patients were enrolled through convenience sampling until the target sample was reached. Because recruitment was nonprobabilistic, the calculated precision represents a planning assumption rather than a guaranteed margin of error for the wider patient population.

Eligibility Criteria:

Women aged 18 years or older were eligible if they had a histologically confirmed diagnosis of breast cancer, had undergone mastectomy and subsequently completed radiotherapy, were able to

participate in the study assessments, and agreed to enrollment. Patients were excluded if they had active metastatic disease, an acute illness or recent hospitalization likely to substantially alter muscle function or body composition, a pre-existing neuromuscular disorder with a major effect on strength, or a condition that prevented valid assessment of muscle strength or body composition. Patients with incomplete treatment records or missing measurements required to classify sarcopenia were also excluded from the primary analysis. Pre-existing sarcopenia was not, by itself, an exclusion criterion: excluding such patients without a reliable pre-radiotherapy assessment would distort the post-treatment proportion. Where prior muscle assessments were available, they were documented separately to help distinguish pre-existing impairment from changes observed after treatment.

Study Procedures:

Demographic and clinical information was obtained through patient interviews and medical records using a standardized data form. Recorded variables included age, height, weight, body mass index, smoking status, menopausal status, relevant chronic conditions, and medication use. Breast cancer characteristics included histological type, stage, tumor receptor status when available, date and type of mastectomy, and receipt of neoadjuvant or adjuvant chemotherapy, endocrine therapy, or other systemic treatment. Radiotherapy records were reviewed for the treated anatomical regions, treatment technique, prescribed total dose, number of fractions, treatment dates, and interval between the final radiotherapy session and study assessment. These variables examined as potential correlates of muscle status, while recognizing that treatment exposures could overlap. At the study visit, muscle strength, muscle quantity, and physical performance assessed using a consistent protocol. Handgrip strength recorded in kilograms with a calibrated dynamometer, and appendicular skeletal muscle mass measured and divided by height squared to obtain the appendicular skeletal muscle index. Usual gait speed recorded as a measure of physical performance. Sarcopenia classified according to the revised European Working Group on Sarcopenia in Older People (EWGSOP2) framework: low muscle strength indicated probable sarcopenia, low muscle quantity together with low strength confirmed sarcopenia, and additional impairment in physical performance indicated severe sarcopenia. For women, the EWGSOP2 handgrip threshold is less than 16 kg; if appendicular muscle mass was measured by dual-energy X-ray absorptiometry, the corresponding index threshold is less than 5.5 kg/m². The final manuscript should state the actual device, measurement protocol, and muscle-mass threshold used at the hospital rather than retain an instrument or threshold that was not used.

Statistical Analysis:

Continuous variables were summarized as means and standard deviations, consistent with the stated assumption of normally distributed data, and categorical variables as frequencies and percentages. The proportion of participants with confirmed sarcopenia was reported with a 95% confidence interval. Mean values were compared between two groups using the independent-samples t test and across more than two groups using one-way analysis of variance, with post hoc comparisons when appropriate. Associations between categorical variables were assessed using the chi-square test or Fisher's exact test when expected cell counts were small. Pearson's correlation coefficient was used to examine relationships between normally distributed continuous variables. If the number of sarcopenia cases was sufficient, a parsimonious multivariable logistic regression model was used to explore associations with prespecified clinical variables, with results expressed as adjusted odds ratios and 95% confidence intervals. All tests were two-sided, and a P value below 0.05 was considered statistically significant. Associations were interpreted without making causal claims.

Ethical Considerations:

The study protocol approved by the Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.FMD.REC.1404.058). Participation was voluntary, written informed consent obtained before study-specific assessments. Patient information coded, handled confidentially, participants' decisions about enrollment or withdrawal did not affect their clinical care.

Results

As summarized in Table 1, the study cohort comprised 125 participants, of whom 41 (32.8%) were classified as sarcopenic. Demographic and clinical analyses revealed that patients with sarcopenia were significantly older and presented with a lower body mass index compared to their non-sarcopenic counterparts. Functional assessments demonstrated markedly lower handgrip strength, appendicular skeletal muscle index, and gait speed in the sarcopenic group (all $P<0.001$). Furthermore, sarcopenia was significantly associated with more advanced TNM stage, a history of adjuvant chemotherapy, and more extensive radiotherapy involving both the chest wall and regional lymph nodes. Additionally, the time elapsed since the completion of radiotherapy was significantly longer in the sarcopenic subgroup, suggesting a potential association between extended post-treatment duration and the persistence or progression of muscle wasting in this population.

Table 1. Demographic, Oncologic, and Treatment-Related Characteristics of Patients Stratified by Sarcopenia Status (N=125)

Variables	Total Cohort (N=125)	Non-Sarcopenic (n=84)	Sarcopenic (n=41)	P-value
Age (years), Mean ± SD	52.6 ± 8.4	50.8 ± 7.9	56.3 ± 8.2	0.001
Body Mass Index (kg/m²), Mean ± SD	26.8 ± 3.5	27.5 ± 3.4	25.4 ± 3.3	0.002
Menopausal Status, n (%)	-	-	-	0.012
Premenopausal	47 (37.6)	38 (45.2)	9 (22.0)	-
Postmenopausal	78 (62.4)	46 (54.8)	32 (78.0)	-
Handgrip Strength (kg), Mean ± SD	18.7 ± 4.6	20.8 ± 3.7	14.4 ± 2.5	< 0.001
Appendicular Skeletal Muscle Index (kg/m²), Mean ± SD	5.82 ± 0.74	6.18 ± 0.58	5.08 ± 0.41	< 0.001
Gait Speed (m/s), Mean ± SD	1.04 ± 0.21	1.11 ± 0.18	0.90 ± 0.19	< 0.001
Pathological TNM Stage, n (%)	-	-	-	0.038
Stage I	23 (18.4)	19 (22.6)	4 (9.8)	-
Stage II	64 (51.2)	45 (53.6)	19 (46.3)	-
Stage III	38 (30.4)	20 (23.8)	18 (43.9)	-
Estrogen Receptor Status, n (%)	-	-	-	0.684
Positive	91 (72.8)	62 (73.8)	29 (70.7)	-
Negative	34 (27.2)	22 (26.2)	12 (29.3)	-
Progesterone Receptor Status, n (%)	-	-	-	0.551
Positive	83 (66.4)	57 (67.9)	26 (63.4)	-
Negative	42 (33.6)	27 (32.1)	15 (36.6)	-
HER2 Receptor Status, n (%)	-	-	-	0.428
Positive	31 (24.8)	23 (27.4)	8 (19.5)	-
Negative	94 (75.2)	61 (72.6)	33 (80.5)	--
Type of Mastectomy, n (%)	-	-	-	0.046
Simple Mastectomy	49 (39.2)	38 (45.2)	11 (26.8)	
Modified Radical Mastectomy	76 (60.8)	46 (54.8)	30 (73.2)	-
Neoadjuvant Chemotherapy, n (%)	-	-	-	0.082
Yes	42 (33.6)	24 (28.6)	18 (43.9)	-
No	83 (66.4)	60 (71.4)	23 (56.1)	-
Adjuvant Chemotherapy, n (%)	-	-	-	0.021
Yes	96 (76.8)	60 (71.4)	36 (87.8)	-
No	29 (23.2)	24 (28.6)	5 (12.2)	-
Endocrine Therapy, n (%)	-	-	-	0.493
Yes	89 (71.2)	61 (72.6)	28 (68.3)	-
No	36 (28.8)	23 (27.4)	13 (31.7)	-
Total Radiotherapy Dose (Gy), Mean ± SD	49.8 ± 3.4	49.4 ± 3.6	50.6 ± 2.8	0.061
Fractionation Schedule, n (%)	-	-	-	0.114
Hypo fractionated (40 to 42.5 Gy in 15 to 16 fractions)	54 (43.2)	40 (47.6)	14 (34.1)	-
Conventional Fractionation (50 Gy in 25 fractions)	71 (56.8)	44 (52.4)	27 (65.9)	-
Radiotherapy Field Extent, n (%)	-	-	-	0.019
Chest Wall Alone	51 (40.8)	40 (47.6)	11 (26.8)	-
Chest Wall and Regional Lymph Nodes	74 (59.2)	44 (52.4)	30 (73.2)	-
Interval from Radiotherapy Completion (months), Mean ± SD	7.4 ± 3.8	6.5 ± 3.2	9.2 ± 4.3	< 0.001

SD, standard deviation; Gy, Gray; TNM, tumor-node-metastasis; HER2, human epidermal growth factor receptor 2. P-values derived from the independent-samples t-test for continuous variables and the Pearson chi-square test or Fisher's exact test for categorical variables.

As demonstrated in Figure 1, the appendicular skeletal muscle index differed significantly according to the extent of the irradiated field, with

patients receiving combined irradiation to the chest wall and regional lymph nodes exhibiting a markedly reduced median muscle index compared to those treated with chest wall irradiation alone. In the regional irradiation cohort, the interquartile range shifted downward, and a substantial density of individual data points clustered below 5.5 kg/m², reflecting a higher frequency of clinically low muscle mass. Conversely, patients treated with localized chest wall fields maintained a higher median index near 6.0 kg/m², indicating that comprehensive locoregional nodal radiation therapy is associated with greater systemic skeletal muscle depletion following mastectomy.

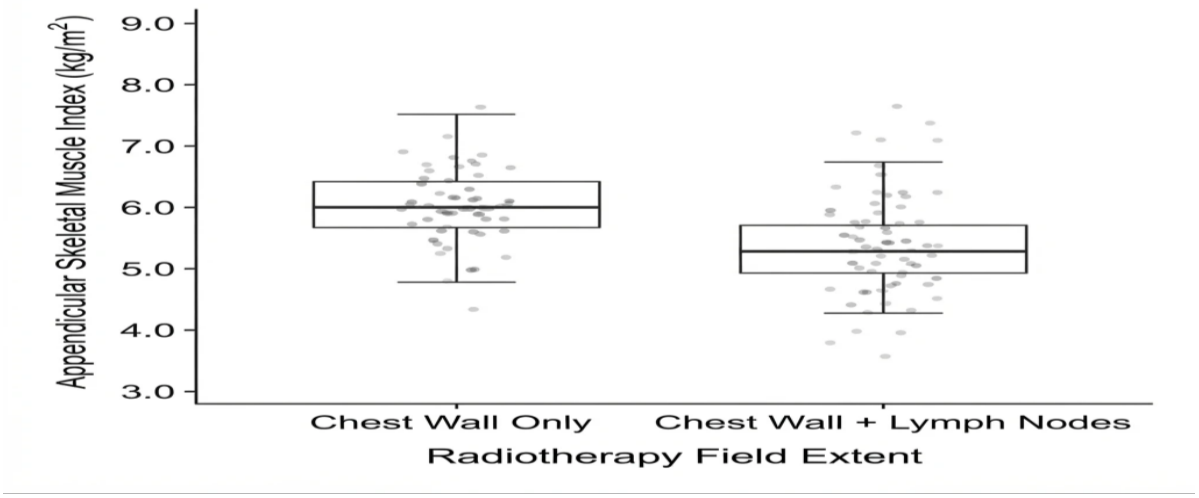


Figure 1. Comparison of Appendicular Skeletal Muscle Index Stratified by Radiotherapy Field Extent

S illustrated in Figure 2, bivariate correlation analysis demonstrated a statistically significant inverse relationship between the time elapsed since radiotherapy completion and the appendicular skeletal muscle index (r=−0.38, P<0.001). Patients assessed at earlier intervals following treatment maintained higher lean muscle mass measurements, whereas individuals evaluated at more extended follow-up durations exhibited a steady, progressive reduction in appendicular skeletal muscle index values. The superimposed linear regression trendline and its 95% confidence interval indicate that longer post-radiotherapy intervals are consistently associated with cumulative muscle mass depletion in post-mastectomy patients.

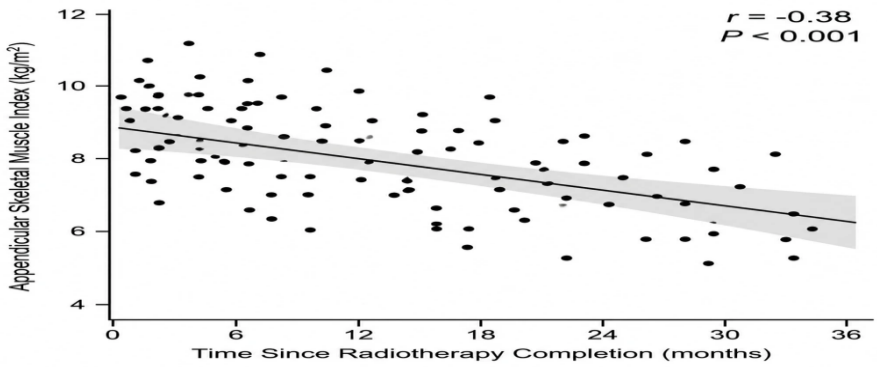


Figure 2. Linear Correlation between Time Elapsed Following Radiotherapy Completion and Appendicular Skeletal Muscle Index

Discussion

Among the 125 patients assessed after mastectomy and radiotherapy, 41 (32.8%) met the study criteria for sarcopenia. Compared with their non-sarcopenic counterparts, they were older and had lower body mass index, handgrip strength, appendicular skeletal muscle index (ASMI), and gait speed. Sarcopenia was also more frequent among patients with advanced pathological stage, adjuvant chemotherapy, and irradiation encompassing both the chest wall and regional lymph nodes. A longer interval since radiotherapy completion was associated with lower ASMI (r = -0.38, P .(٠/٠٠١ > The observed proportion is numerically close to an estimate reported in a breast cancer meta-analysis, although differences in populations and diagnostic methods prevent direct comparison. Together, these findings identify a group with substantial muscle-related impairment, without establishing when that impairment developed [10,11].

The combination of reduced strength and reduced muscle mass is particularly relevant to interpreting these results. Under the revised European Working Group on Sarcopenia in Older People criteria, low strength raises suspicion of sarcopenia, while low muscle quantity confirms the diagnosis; impaired physical performance indicates greater severity. The lower gait speed observed here therefore adds functional context to the differences in handgrip strength and ASMI. Nevertheless, because strength and muscle mass contributed to the classification of patients, their marked differences between the two groups are partly expected by definition. They should not be interpreted as independent evidence that radiotherapy caused muscle loss. Studies in women with breast cancer have likewise emphasized assessing muscle function alongside body composition rather than relying on a single measurement [12,13].

Older age and postmenopausal status were more common in the sarcopenic group, suggesting that vulnerability present before radiotherapy may have contributed to the findings. Age-related changes in muscle, differences in habitual activity, and the cumulative effects of cancer treatment offer plausible explanations, but none was tested mechanistically in this cohort. Menopausal status may also reflect age and treatment history rather than an independent biological effect. Previous longitudinal work has shown that body composition can change around breast cancer treatment, although the magnitude and direction of those changes are not uniform across studies. Research in premenopausal patients receiving chemotherapy has additionally linked treatment-related changes in body composition with reduced physical activity. Baseline measurements would be needed to distinguish these potential pathways in the present patients [14,15].

Although mean body mass index was lower among patients with sarcopenia, body mass index alone cannot adequately characterize skeletal muscle. Patients with similar weight may differ considerably in their proportions of muscle and adipose tissue, and muscle loss can coexist with stable or increasing weight. In a large cohort of women with nonmetastatic breast cancer, computed tomography-derived body-composition measures provided information not captured by body mass index. A separate study of neoadjuvant chemotherapy found that changes in muscle obscured when assessment focused on body size rather than muscle mass. Accordingly, the present association between lower body mass index and sarcopenia should not lead clinicians to exclude patients with higher body mass index from muscle assessment [16,17].

The associations with advanced pathological stage and modified radical mastectomy require particular caution. Patients with more advanced disease may receive more intensive combinations of surgery, systemic therapy, and regional nodal irradiation. Consequently, these characteristics may be markers of treatment burden or underlying disease severity rather than separate causes of sarcopenia. Current postmastectomy radiotherapy guidance links regional nodal treatment to oncological indications, particularly nodal involvement and other high-risk features. Randomized evidence also demonstrates the clinical importance of appropriate nodal irradiation for selected patients. The lower muscle measurements observed in the more extensively irradiated group must therefore be interpreted alongside the reasons those patients received broader treatment. Without adjustment for stage, nodal status, surgery, and systemic therapy, an effect attributable specifically to radiation-field extent cannot be isolated [18,19].

The higher frequency of adjuvant chemotherapy in the sarcopenic group provides another possible explanation for the observed muscle differences. Chemotherapy may coincide with fatigue, reduced activity, nutritional difficulties, and changes in body composition; however, treatment effects vary by regimen and individual circumstances. In a trial conducted during breast cancer chemotherapy, both intervention and control groups lost fat-free mass, while supervised strength training improved strength without clearly preventing that loss. A prospective observational study also documented declining lean tissue during chemotherapy, alongside changes in fluid distribution that complicated interpretation of body-composition measurements. These findings support chemotherapy as a potential contributor, not a proven cause in this cohort. Treatment regimen, cumulative exposure, nutritional status, and pretreatment muscle measurements would help clarify its contribution [20,21].

The lower ASMI shown for patients receiving chest-wall and regional nodal irradiation is clinically noteworthy, but the biological explanation remains uncertain. Breast radiotherapy can affect tissues within the treated field: longitudinal imaging has documented changes in pectoral muscle volume, and a smaller prospective series identified changes in pectoralis major stiffness and thickness after treatment. Such localized findings make treatment-related muscular morbidity plausible, particularly when larger anatomical regions are exposed. They do not, however, demonstrate that nodal irradiation directly reduces appendicular muscle mass throughout the body. Indirect pathways, including pain, restricted movement, fatigue, or reduced participation in exercise, are possible but not measured here. Moreover, the cited muscle-imaging studies largely involved breast-conserving treatment, so their findings cannot be assumed to apply unchanged after mastectomy [22,23].

The inverse association between time since radiotherapy and ASMI warrants similarly

restrained interpretation. Patients assessed later had lower muscle measurements, but each participant evaluated at only one point in time. The correlation therefore does not demonstrate progressive decline within individuals, persistence of treatment-related injury, or an effect of elapsed time itself. Differences in age, initial muscle reserve, treatment intensity, or subsequent activity could also influence the pattern. In a prospective breast cancer cohort, certain radiotherapy characteristics were associated with fatigue at one year, illustrating a possible route through which recovery and activity affected. Conversely, a study of nodal irradiation did not find worse patient-reported arm outcomes with hypofractionation than with conventional schedules. Neither finding establishes the mechanism of the present ASMI association [24,25].

The lack of statistically significant differences for receptor status, total radiation dose, and fractionation schedule not taken as proof that these factors have no relationship with muscle health. Some comparisons may have limited power, while total prescribed dose does not describe the exposure of individual muscles or other normal tissues. The clinical importance of identifying functional problems nevertheless remains clear. Trials involving women receiving breast radiotherapy have found that exercise interventions can improve fatigue-related outcomes, including recovery after treatment. A randomized trial of resistance training during adjuvant radiotherapy also reported benefits for physical fatigue and selected quality-of-life measures. These studies support offering appropriate rehabilitation when indicated, but they do not show that exercise would eliminate the associations observed in this cross-sectional cohort [26, 27]. This study's assessment of muscle quantity, strength, and walking performance offers a broader view than body mass index alone. Its principal limitations are the single-center convenience sample, absence of pretreatment measurements or a nonirradiated comparison group, and reliance on unadjusted associations. The design measures sarcopenia prevalence at assessment, not its incidence after radiotherapy; the manuscript title should be revised unless longitudinal data are available. Prospective studies should measure muscle function before treatment and repeatedly afterward while accounting for stage, chemotherapy, radiation-field extent, nutrition, and physical activity. Meanwhile, individualized assessment and rehabilitation are reasonable clinical considerations: randomized studies suggest that progressive resistance exercise can preserve appendicular muscle mass or improve strength in breast cancer populations. These interventions should be evaluated against outcomes measured in the patients most at risk [28,29].

Conclusion

Post-mastectomy radiotherapy, particularly comprehensive regional nodal irradiation and extended post-treatment duration, is significantly associated with a high prevalence of sarcopenia and progressive skeletal muscle depletion. These findings underscore the critical clinical necessity for routine muscle mass screening and targeted rehabilitation protocols in survivors undergoing locoregional radiotherapy.

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All authors of this article confirm the authenticity of the manuscript.

Conflicts of interest

The authors declare that they have no competing interests.

Disclosure Statement

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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